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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,801	04/18/2005	Margaret Hopwood	PA/4-32730A	3682

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ONE HEALTH PLAZA 104/3
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EXAMINER	
HOUGHTLING, RICHARD A	

ART UNIT	PAPER NUMBER
4133	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,801	HOPWOOD ET AL.	
	Examiner	Art Unit	
	Richard A. Houghtling, Ph.D.	4133	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-9 and 12-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-9, 12-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *18 April 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 4-9 and 12-16 are pending in this application and are examined on their merits, herein. The Examiner acknowledges receipt of a preliminary amendment filed on April 18, 2005 in which applicants canceled claims 2-3 and 10-11.

Priority

2. Applicants' claim to foreign priority is acknowledged; and, two applications from Great Britain (GB 0224199.0 and GB 0224200.6) were entered into the record.

Information Disclosure Statements

3. Receipt of an information disclosure statement filed by applicants on April 18, 2005 is acknowledged; examiner entered the disclosure into the record and references were considered.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition and a method for

therapeutic treatment of pain, does not reasonably provide enablement for both prophylactic and preventative treatment as well as curative pain treatment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Within applicants' specification, the terms, "treatment" or "treat," are given special meaning, contrary to the accepted meaning such that the new definition of treatment further includes prophylactic or preventive treatment, as well as, curative of pain suffering (see col. 2, lines 12-14).

According to Stedman's Concise Medical Dictionary (1987), the term "prophylactic" is defined as 1) preventive, preventing disease or 2) an agent that acts as a preventive against disease (p. 613, col. 2, lines 35-41); while, "preventive" is defined as 1) prophylactic 2) anything that arrests the threatened onset of disease (p. 607, col.2, lines 53-56). Using the common medical definitions of prophylaxis as preventive, applicants' specification fails to provide enough detailed teachings for an artisan to make and use the invention commensurate within the scope of the claims.

The instant claims 4 and 12 and are drawn to a method for the treatment of pain to patients suffering therefrom and administering a composition comprising a combination of oxcarbazepine or its derivative and a cyclooxygenase-2 inhibitor.

Because applicants' elected to provide "special definitions" for the terms, "treatment" or "treat," which includes treatment of patients at risk of suffering pain or patients already suffering pain in such a way that the disease modifying treatment includes prophylactic or preventive treatment, as well as, curative of suffering pain (see col. 2, lines 12-14). The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdAPIs 1986) at 547 the court recited eight factors:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Nature of the invention: The instant invention pertains to a method for prophylaxis, prevention or curing a condition whereby a patient is suffering from pain.

State of the art: The skilled artisan would view that prevention of pain in animals totally, absolutely, or permanently, so as to not even occur the first time is highly unlikely.

Relative skill of those in the art: The relative skill of those in the art is high, typically requiring an advanced professional degree.

Predictability or lack thereof in the art: The skilled artisan would view that treatment to prevent a patient suffering from pain so as to be totally, absolutely, or permanently, as highly unpredictable, and so as to not even occur at the first time, is highly unpredictable.

Amount of guidance provided by the inventor and existence of working examples: In the instant case, 12 working examples are provided in the specification as filed showing how to formulate pharmaceutical compositions and 1 working example provides a protocol for a clinical study, however, no working examples are provided or teachings as to the methods of preventing patients from suffering pain, nevertheless, methods to not suffer it in the first place, or teachings of how to know that a patient suffering pain is protected after drug treatment such that the treatment was so totally, absolutely, or permanently, so as to not even occur the first time. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP §2164.

Genetech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague limitations of general ideas that may or may not be workable.

Therefore, in view of the Wands factors, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test the method in the instant claim as to whether prevention of pain suffering in a patient in need thereof administered an oxcarbezpine of Formula I or II, such as a human would do so totally, absolutely, or permanently, with no assurance of success.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coe et al. (US PGPublication 2001/0036943).

Applicants' invention is drawn to a combination of oxcarbazepine and a cyclooxygenase-2 (COX-2) inhibitor. Claims are drawn to pharmaceutical compositions, methods for treatment and a packaged product. Specifically, two formulations of oxcarbazepine are provided, Formula I corresponds to two chemical structures—oxcarbazepine or 10,11-dihydro-10-hydroxy-5H-dibenz[b,f]azepine-5-carboxamide (MHD), whereas Formula II encompasses the structures of Formula I and also carbamazepine. Similarly, two formulations of the COX-2 inhibitor (Formula V or VI) are also claimed. The distinction between Formula V and Formula VI is the presence or absence of pharmaceutically acceptable salts, respectively.

The instant composition of claim 9 and the method of claim 12 thus comprise: oxcarbazepine, carbamazepine or MHD (and a COX-2 inhibitor without pharmaceutically acceptable salts.

Coe et al. teaches pharmaceutical compositions and methods for treatment of acute, chronic and/or neuropathic pain with reduced nausea and upset stomach (abstract; col. 1, lines 28-32 ¶ [0001]; col. 7, ¶ [271]; col. 16-17 claims 17-18 and 21 or 26). The pharmaceutical composition of Coe et al. comprises a therapeutically effective combination of a nicotinic receptor partial agonist, an analgesic agent and a pharmaceutically acceptable carrier (col. 1, ¶ [0004])). The list of analgesic agents includes: a COX 1 inhibitor such as salycylic acid (aspirin), diclofenac, oxicams, indomethacin, ibuprofen, and naproxen; a COX 2 inhibitor such as rofecoxib or celecoxib; and an anti-convulsants such as gabapentin, carbamazepine, pregabalin, topiramate and valproic acid (col. 4, ¶ [0138], lines 50-55). Finally, Coe et al. teaches a method for treating a disorder or condition involving pain which predominates from acute pain, chronic pain, neuropathic pain and migraine which further includes soft tissue and peripheral damage (col. 7, ¶ [271]) comprising administering to a mammal a pain attenuating effective amount of a pharmaceutical composition comprising: a nicotinic receptor partial agonist, an analgesic agent, and a pharmaceutically acceptable carrier, using effective amounts of nicotinic receptor partial agonist and analgesic agent

so as to provide an effective composition for the treatment of acute chronic and/or neuropathic pain and migraine (col. 7, ¶ [0271] to ¶ [0273]).

The instant pharmaceutical compositions claimed by applicant are quite similar in scope to those taught by Coe et al. Specifically, applicants' claims 9 and 12 are drawn to oxcarbazepine of Formula I which includes the chemical structures of oxcarbazepine, carbamazepine and MHD is clearly taught in the composition by Coe et al. At the time of applicants' invention, one of ordinary skill in the art would have found it *prima facie obvious* to include both the COX-2 inhibitor and carbamazepine with the nicotinic receptor partial agonist. Within the art, it is widely accepted that inclusion of more than one pharmaceutical agent having similar pharmacological effect when combined, results in additive effects. Thus, one of ordinary skill in the art seeking to increase the marketability of the Coe et al. composition by further comprising additional agents known to have analgesic effects so as to better treat patients with different types of neuropathic pain would have had a reasonable chance of success at making applicants' instant compositions of claims 9 or 12 by use of routine experimentation and optimization strategies. In doing so, one of ordinary skill in the art would have used the list of analgesic drugs taught by Coe et al. such as, opioids, COX-2 inhibitors, NMDA receptor antagonists, anticonvulsants, and tricyclic antidepressants and would have had a reasonable expectation of success at reaching the instant compositions claimed by applicants.

6. Claims 1, 4-8, 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coe et al. (U.S. PGPub 2001/0036943) as applied to claims 9 and 12 above, Kiguchi et al. (2001) and Pro Health Arthritis Support website (October 4, 2002).

The instant composition of claim 1 and the method of claim 4 thus comprise: oxcarbazepine or MHD and a COX-2 inhibitor with pharmaceutically acceptable salts.

Specifically, applicants' invention is drawn to a pharmaceutical composition (claim 1), which is further limited to rofecoxib, etoricoxib, celecoxib, valdecoxib, parecoxib, and a 5-alkyl-2-arylaminophenylacetic acid derivative or a pharmaceutically acceptable salt or any hydrate thereof as the COX-2 inhibitor (claim 6); or a COX-2 inhibitor or its pharmaceutically acceptable salts (claim 7) that is further limited to 5-methyl-2-(2'-chloro-6'-fluoroanilino)phenylacetic acid or a pharmaceutically acceptable salt or ester thereof (claim 8). Likewise, the composition of claim 9 is further limited to the COX-2 inhibitor which is 5-methyl-2-(2'-chloro-6'-fluoroanilino)phenylacetic acid (lumiracoxib) or a pharmaceutically acceptable salt or ester thereof (claim 14), the carbamazepine derivative is oxcarbazepine (claim 15) or is 10,11-dihydro-10-hydroxy-5H-dibenz[b,f]azepine-5-carboxamide (MHD).

Coe et al. teach compositions and methods for treatment of pain as discussed above. Coe et al. does not teach, oxcarbazepine or its metabolite (MHD) or 5-methyl-2-(2'-chloro-6'-fluoroanilino)phenylacetic acid as the COX-2 inhibitor in either the pharmaceutical composition or the method.

Kiguchi et al. teach both oxcarbazepine and its metabolite MHD as effective agents for treatment of neuropathic pain (p. 174, Discussion, ¶ 8-9). Using a model system that assesses nociceptive transmission of primary afferent C-fibers to secondary neurons in the trigeminal subnucleus caudalis. Kiguchi et al. teach that intravenous administration of oxcarbazepine or MHD effectively reduced neurotransmission (see p. 171, Figures 4-5; p. 172, Figure 7; and p. 173, 3rd ¶). Central microinjection of MHD also had a similar effect, which was almost as effective as the art-recognized analgesic drug standard—morphine (see p. 172, Figure 6; p. 173, 4th ¶). However, Kiguchi et al. does not teach a COX-2 inhibitor or combination therewith.

In the article posted on the proHealth Arthritis Support website posted October 4, 2002, lumiracoxib is described as an investigational COX-2 selective inhibitor that had efficacy equal to the current European "gold standard," diclofenac, in the treatment of patients with arthritis and pain (1st ¶, lines 3-6). This article does not teach an anticonvulsant or the combination therewith.

Taken together, the teachings of Coe et al., Kiguchi et al., and the article from the arthritis support.com website, each teach a pharmaceutical agent which is known individually in the prior art to have the same therapeutic effect (treating pain), thus, it is obvious to one having ordinary skill in the art to combine these teachings in order to form a third composition to be used for the very same purpose (to treat pain). Without any evidentiary support of unexpected results or findings by the combination of the two known compositions, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to combine these two teachings, thus resulting in applicants' claimed composition. The basis for this *prima facie* obviousness rejection can be found in the following case law:

> "It is however, *prima facie* obvious to combine two compositions taught in the prior art useful for the same purpose, in order to form a third composition to be used for the very same purpose...[T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069,1072 (CCPA 1980).

Finally applicant is advised in regards to claims 5 and 13, each of which is drawn to a package, that instructions for use carry no patentable weight.

Conclusion

In conclusion, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard A. Houghtling, Ph.D. whose telephone number is 571-272-9334. The examiner can normally be reached Monday to Thursday from

8:00 am - 5:00 pm. The examiner can also be reached on alternate Fridays (9 am – Noon).

The Group 1600 fax phone number where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on 571-272-0911.

Richard A. Houghtling, Ph.D.

JEFFREY STUCKER
SUPERVISORY PATENT EXAMINER